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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,852	11/04/2003	Susumu Hirose	244855US0	5771

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,852	HIROSE ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/04/03 has been acknowledged.

Claims 1-4 are pending and are examined in this office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siden et al, Methods. 17(2):112-124, 1999) in view of Saffrin et al (US 4,868,311, 1989) and Chevalier et al (J Histochem. Cytochem. 45(4):481-91, 1997).

Invention is drawn to a method for detecting negatively supercoiled DNA in a cell using a biotinylated psorlan probe.

Siden et al teaches use of psoralen cross-linking as probe of torsional tension and topological domain size in vivo. The cited art further teaches a protocol for measuring super-coiled DNA by treating cells with 313nm UV light and Me3-psoralen (page 116 col.2, table-1). The cited art further teaches that the binding constant intercalating agents such as psoralen and ethidium bromide are proportional to the level of negative supercoiling and there exists a linear correlation between photobinding of psoralan and negative superhelical density. The cited art further teaches that to determine superhelical density in-vivo, measurement of psoralen binding to DNA can be achieved by quantitating the incorporation psoralan into total genomic DNA (page 113, col.2, para.2-3). The cited art further teaches measurement of topological domain size by measuring R1/N values (page 114, col.1 para. 2-3; page 122, fog-3). Even though

Siden teaches use of Me3-psoralen for the quantitation of super coiled DNA the cited art does not teaches the use of biotinylated pspralen.

Saffrin et al teaches biotinlayted-psoralen (BPsor) which cross-links to DNA in the presence of UV rays (col. 9, lines 45-55). The cited art further teaches that BPsor binds covalently to DNA in a near UV photoreaction, resulting in interstrand crosslinks, and like other biotinylated molecules it binds to avidin, even after it has been incorporated into DNA. The cited art further teaches that the biotinylation does not interfere with its biological activity in lymphocytes. The cited art further teaches that the delivery of BPsor to cells as an avidin-BPsor conjugate (col. 5 lines 12-34; col.12 lines 24-68). The cited art further teaches the detection of cross-linked DNA using biotin-avidin based ELISA system (col.11 lines 23-51).

Chevalier et al provides a review for in situ hybridization (ISH) techniques using biotinylated probes. The cited art further teaches that biotin, a small vitamin molecule (M_r 244), binds with high affinity to avidin, a protein largely distributed in egg whites (M_r 70,000), which can be conjugated to different markers such as fluorescent dyes, peroxidase, ferritin, and colloidal gold (page 482, col.1 para.3). The cited are further teaches permeabilization of cells or tissue section using permeation-promoting agent (page 484, col.1 para.2; page 488, col.1 para. 4). The cited art further teaches the detection of tissue or cells containing DNA of interest using biotinylated probes (see Fig. 4-6).

Thus it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the invention of Siden by substituting the Me3-psoralen with biotinlayted-psoralen (BPsor) for in situ detection of DNA. One would have been motivated to do so because biotin-avidin system provides flexibility in the selection of different diagnostic labels. One would have a reasonable expectation of success, since the use of biotin-avidin system for intra cellular detection of target moieties has been routine in the art at time the instant invention was made. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

-sk

SUMESH KAUSHAL
PATENT EXAMINER